Cobination vaccines make life easier for our patients. But until the payment and regulatory issues are resolved, the same is not true for us. In January, the Food and Drug Administration’s Vaccines and Related Biological Products Advisory Committee considered the overall safety and efficacy of Sanofi Pasteur’s Pentacel, a combination vaccine containing diphtheria, tetanus toxoid, and acellular pertussis (DTPa), inactivated polio (IPV), and Haemophilus influenzae type b (Hib). If approved, this vaccine will compete with GlaxoSmithKline’s Pediarix, which contains DTPa, IPV, and hepatitis B antigens.

Infants given a dose of hepatitis B (HBV) vaccine at birth and then Pentacel at 2, 4, and 6 months of age would not be receiving an extra dose of HBV vaccine, as they would with Pediarix. Some see this as an advantage to Pentacel, but my colleagues and I showed that the extra HB dose was not a problem in terms of reactogenicity or immunogenicity, even though it resulted in considerably higher anti-HB levels (Pediatr. Infect. Dis. J. 2002;21:854-9).

Pediarix is now widely used in the public sector through the Vaccines for Children Program. In that setting, it has resulted in improved immunization rates and reduced errors. But the private sector has been slower to adopt Pediarix, and I predict that the same will be true of Pentaclave for the same reason: The current lack of appropriate licensure of the vaccine against lesions—6 CIN/AIS and 2 vulvar/vaginal cases, all within 1 day of receiving Gardasil—caused by nonvaccine strains of HPV.

Infectious Diseases

Are Combo Vaccines Really Simpler?

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Gardasil Efficacy Is Looking Better and Better With Time

BY MIRIAM E. TUCKER
Senior Writer

ATLANTA — The efficacy of Gardasil is becoming more apparent over time, Dr. Elav Barr said at a meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention.

Merck is continuing to subjects post marketing, with nearly 3 years of data now available from three of the pre-marketing trials involving more than 18,000 young women. Among those are 2.4 years for the group that was naive to all four vaccine strains of human papillomavirus (6, 11, 16, and 18) at baseline. 2.9 years for another group that was naive to 14 HPV types, and 2.8 years for a combined group of uninfected and infected women at baseline, said Dr. Barr. The program head of HPV Vaccines for Merck Research Laboratories, Blue Bell, Pa.

In the peer-review protocol investigation comparing only those naive to the vaccine HPV strains, efficacy of the vaccine against HPV 16/18-related cervical intraepithelial neoplasia (CIN) 2/3 or adenocarcinoma in situ (AIS) is 99%, down from 100% at the time of licensure. The drop was the result of just one case of HPV 16/18-related CIN3 in a Gardasil recipient (versus 73 cases in the placebo group). An investigation into one case of AIS determined that it was likely caused by contamination, Dr. Barr said.

Efficacy against HPV 16/18-related vulvar and vaginal intraepithelial neoplasia 2/3 remains at 100%, as it was at licensure. Efficacy against any grade of HPV 16/18-related CIN or AIS is now at 96%, compared with 95% at licensure. Efficacy continues to increase over time as more cases of HPV 16/18-related disease occur in placebo recipients. Against all viral and vaginal lesions, including warts, the vaccine has stayed 99% effective. It’s possible that the few vaccine recipients who developed lesions—6 CIN/AIS and 2 vulvar/vaginal lesions, compared with 148 and 189, respectively, among placebo recipients—were already infected at baseline, he noted.

In the combined group of those infected and uninfected at baseline, vaccine efficacy is now 41% against CIN 2/3 or AIS (versus 34% at licensure), 71% against vaginal or vulvar intraepithelial neoplasia, 99% against AIS (2/3 at licensure), 54% against CIN of any grade (46% at licensure), and 78% against vulvar/vaginal lesions including warts, just from 70%.

A preliminary data also suggest cross-protection of the vaccine against lesions caused by nonvaccine strains of HPV.

Injection Site Pain Is Gardasil’s Most Frequent Adverse Event

BY MIRIAM E. TUCKER
Senior Writer

ATLANTA — Injection site pain is the most frequently reported adverse event following receipt of the quadrivalent human papillomavirus vaccine, Dr. Lauri Markowitz said at a meeting of the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices.

Through January 2007, the passive Vaccine Adverse Event Reporting System (VAERS) has received a total of 542 reports associated with Merck’s quadrivalent human papillomavirus (HPV) vaccine (Gardasil), of which 5% were considered serious. No deaths were reported, said Dr. Markowitz of the CDC’s National Center for HIV, STD, and TB Prevention.

A total of 2.1 million doses of Merck’s HPV vaccine had been distributed through December 2006. The adverse event reporting rate, 25,100/100,000 doses, is slightly higher than that seen with other vaccines but “not unexpected for a new vaccine,” she noted.

Injection site pain was the most commonly reported adverse event (18%), followed by dizziness (11%), syncope (11%), fever (9%), and nausea (9%). More than 99% occurred in females, reflecting the population for whom the vaccine currently is recommended. Nearly half (47%) of the reporting adverse events were aged 13-18 years, and another 38% were aged 19-26 years. Only 7% were aged 9-12 years, 6% were over 26 years of age, and the rest were less than 9 years.

There were three reported cases of Guillain-Barré syndrome (GBS), two of whom had simultaneously received the meningococcal conjugate vaccine (Menactra) 9 and 13 days earlier. It was not known whether the third GBS case had received other vaccines at the same time. An association between Menactra and GBS has been reported, although it is not yet clear whether the relationship is causal (MMWR 2006;55:1120-4).

Facial palsy was also reported in two cases, all within 1 day of receiving Gardasil. Two of those individuals had received influenza vaccine—one live attenuated and one inactivated—at the same time. The background rate of facial palsy in the general population is 10/100,000 per year.

Physicians are encouraged to report all clinically significant adverse events in patients following receipt in VAERS, online at www.vaers.hhs.gov, by phone at 800-822-7967, or by fax at 877-721-0366.